Remarks

Claims 14-17 and pending and rejected. Claims 14 and 32 are amended and new claims 33 and 34 are added in response to the rejections under the judicially created obviousness type double patenting and 35 U.S.C. 102(b) and 103, as discussed below. Support is found at least in the original claims and at p. 12, line 1 to p. 14, line 13; p. 12, lines 19-22; p. 13, lines 15-19; and p. 23, lines 14-30.

Double patenting

Claims 14-17 were rejected under the judicially created doctrine of obviousness-type double patenting as unpatentable over claims 1-4 of U.S. Patent No. 5,906,828 ("the '828 patent"). Claim 32 was rejected under the judicially created doctrine of obviousness-type double patenting over claim 20 of U.S. Patent No. 6,045,818 ("the '818 patent"). Applicants respectfully traverse the rejections if they are applied to the claims as amended and the new claims 33 and 34.

Claims 1-4 of the '818 patent define a method of growing eukaryotic cells which includes the following steps:

(a) bringing into contact the cells and a composition comprising (1) a biocompatible solid substrate, (2) biocompatible branched water soluble polymeric tethers, and (3) growth effector molecules, wherein one end of each tether is covalently linked to the substrate, each tether is able to covalently link more than one growth effector molecule, each growth effector molecule is covalently linked to a distal end of a tether so that the growth effector molecule cannot be

internalized by cells attached to the substrate, and the growth effector molecules are attached to the substrate in a concentration effective to enhance the rate of target cell growth over the rate of target cell growth with soluble growth effector molecules and growth effector molecules adsorbed to a substrate, without internalization of the molecules; and

(b) maintaining the contacting cells and composition under conditions and for a time sufficient to cause the cells to grow; wherein the step of bringing into contact comprises administering the composition to a patient in need of cell growth.

Claim 20 of the '818 patent defines a method of testing a compound for an effect on tissue. The method recites the following steps:

(a) bringing into contact the compound to be tested and a composition comprising (1) a biocompatible solid substrate, (2) biocompatible branched water soluble polymeric tethers comprising a polymeric material selected from the group consisting of polyethylene oxide, polyvinyl alcohol, polyhydroxyalkyl (meth)acrylate, polyacrylamide, and starches, (3) growth effector molecules, and (4) growing cells, wherein one end of each tether is covalently linked to the substrate, each tether is able to covalently link more than one growth effector molecule, each growth effector molecule is covalently linked to a distal end of a tether so that the growth effector molecule cannot be internalized by cells attached to the substrate, the growth effector molecules are attached to the substrate in a concentration effective to enhance the rate of target cell growth over the rate of target cell growth with soluble growth effector molecules and growth

effector molecules adsorbed to a substrate, without internalization of the molecules, and wherein the growing cells are bound to the growth effector molecules;

(b) incubating the compound and the composition under conditions promoting cell growth; and

(c) observing the cells for any effect not observed in cells not brought into contact with the composition,

wherein the substrate has one of the following materials: glasses, metals, polystyrenes, polyethylene vinyl acetates, polypropylenes, polymethacrylates, polyacrylates, polyethylenes, polyethylene oxides, polysilicates, polycarbonates, polytetrafluoroethylene, fluorocarbons, nylon, silicon rubber, polyanhydrides, polyglycolic acids, polyhydroxyacids, polyesters, polycapralactone, polyhydroxybutyrate, polyphosphazenes, polyorthoesters, polyurethanes, and combinations thereof.

Claims 14-17 and 32, as amended, and new claims 33 and 34 define methods that require the tether to be covalently linked to the substrate and the growth effector molecule by attachment agents which are the same. This limitation is absent from claims 1-4 of the '828 patent and claim 20 of the '818 patent. As WO 89/05616, the reference cited by the Examiner, clearly indicates, the nature of the linking agent plays an important function in directing the orientation and spacing of the tether and the attached growth effector molecules, which is important for obtaining a substantially optimum activity of the growth effector molecule (see, for example, p.

14, lines 1-19 of WO 89/05616, discussed below). Claims 1-4 of the '828 patent and claim 20 of the '818 patent clearly do not recite nor make obvious this important feature.

The Examiner conceded that the nature of the linking agent plays an important function in directing the orientation and spacing of the tether and the attached growth effector molecule, which is important for obtaining a substantially optimum activity of the growth effector molecule. The Examiner nonetheless alleged that the claims failed to recite such optimum activity of the growth effector molecule. This assertion is baseless. As WO 616, the prior art reference makes clear, the optimum activity of the growth effector molecule results from the orientation and spacing of the tether and the attached growth effector molecule, which is controlled substantially by the linking agents (see the discussion of WO 616 below). Therefore, optimum activity of the growth effector molecule is an inherent result of the method using the same attachment agent to link the tether to the substrate and the growth effector molecule.

Therefore, the obviousness-type double patent rejections are inappropriate as applied to the amended claims 14-17 and 32.

Rejection Under 35 U.S.C. § 102

Claims 14-17 were rejected under 35 U.S.C. § 102(b) as anticipated by WO 89/05616 by Bio-Metric Systems, Inc. ("WO 616"). Applicants respectfully traverse this rejection to the extent that it is applied to the claims as amended.

WO 616

WO 616 describes biocompatible coatings formed of (1) a biomolecule, (2) a spacer, and (3) a support surface (p. 4, lines 8-16). The support surface is preferably formed of a biomaterial defined at p. 8, line 32 to p. 9, line 16, and is characterized as "relatively hydrophobic." (p. 8, lines 1 and 2). **The spacer is required to have two linking groups or reactive groups that are different from one another** (p. 10, lines 1-6). The reactive group linking the spacer to the support surface is a hydrophobic (p. 11, lines 11-12), and preferably photochemical group (p. 10, lines 9-10). Indeed, all the chemicals listed as proper groups linking the spacer to the support surface are hydrophobic photochemical groups (p. 10, line 13). The hydrophobic nature of the group linking to the support surface is important in providing the desired orientation of the spacer and the biomolecule attached to the spacer (p. 14, lines 1-17). **Note, WO 616 teaches that the selection of different reactive groups for linking the spacer to the substrate and the biomolecule is important in achieving** (p. 11, line 9 to p. 16, line 3) **the optimum activity of the biomolecule.**

The claimed invention

Claims 14-17, which are amended to depend on the new independent claim 33, in contrast, specifically require the attachment agents covalently coupling the tether (spacer) to the substrate (support surface) and the tether to the growth effector molecule to be the same attachment agents. Claims 14-17, as amended, further require the attachment agent to be one of

cyanogen bromide, succinimide, aldehyde, tosyl chloride, avidin-biotin, epoxide, and maleimide, or carbodiimide.

As discussed above, the method described in WO 616 specifically requires the reactive groups (linking agents) to be different. As discussed above, WO 616 further teaches that the difference between the reactive groups (linking agents) is important in achieving the optimum activity of the biomolecule. Accordingly, WO 616 does not anticipate claims 14-17, as amended, and new claims 33 and 34, which requires the linking agents to be the same.

Rejection Under 35 U.S.C. § 103

Claims 14-17 were rejected under 35 U.S.C. § 103(a) as obvious over WO 616. The applicants respectfully traverse this rejection to the extent that it is applied to the claims as amended.

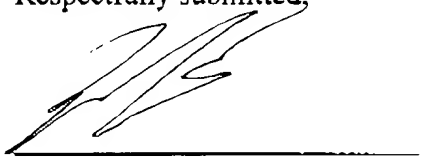
As discussed above, WO 616 defines a method of attaching a biomolecule to a supporting surface via a spacer. The spacer is attached to the supporting surface via a reactive group which is different from a second reactive group attaching the spacer to the biomolecule (p. 10, lines 1-6). WO 616 further teaches that the selection of the reactive groups is important for achieving the optimum activity of the biomolecule attached to the supporting surface (p. 11, line 9 to p. 16, line 3).

In contrast, the claimed method in any of claims 14-17, as amended, and new claims 33 and 34 specifically require the linking agents linking the tether to the substrate and the tether to the growth effector molecule to be the same. Therefore, WO 616 provides no motivation for one

of ordinary skill in the art to arrive at the claimed method. For the same reason, nor would WO 616 lead one of ordinary skill in the art to have a reasonable expectation of success of amended claims 14-17 and new claims 33 and 34. Therefore, WO 616 would not render claims 14-17, as amended, and new claims 33 and 34 *prima facie* obvious under 35 U.S.C. 103 (*see*, *Hodosh v. Block Drug Co., Inc.*, 786 F.2d 1136, 1143 n.5, 229 USPQ 182, 187 n.5 (Fed. Cir. 1986); *see also* MPEP § 2141). Furthermore, in teaching that it is important to use different reactive groups (linking agents) to link the spacer (tether) to the supporting surface (substrate), WO 616 teaches away from the claimed method in the present application.

Allowance of claims 14-17 and 32, as amended, is respectfully solicited.

Respectfully submitted,



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CERTIFICATE OF FACSIMILE TRANSMISSION

I hereby certify that the enclosed Response to Office Action and all documents shown as being attached is being facsimile transmitted to the U. S. Patent and Trademark Office on the date shown below.

Date: May 2, 2003

Peggy Bailey

Peggy Bailey

Marked Up Version of Amended Claims

Pursuant to 37 C.F.R. § 1.121(c)(1)(ii)

14. (Three times amended) ~~A~~ The method of claim 33 ~~for growing eukaryotic cells comprising~~

~~bringing into contact the cells and a composition comprising~~

~~a biocompatible solid substrate,~~

~~biocompatible polymeric tethers, and~~

~~growth effector molecules,~~

~~wherein one end of each tether is covalently linked to the substrate and each growth effector molecule is covalently linked to a distal end of a tether so that the growth effector molecule cannot be internalized by cells attached to the substrate, and the growth effector molecules are attached to the substrate in a concentration effective to enhance the rate of target cell growth without internalization of the molecules; and~~

wherein the ~~one end of each tether covalently linked to the substrate is achieved using an~~ attachment agent is selected from the group consisting of cyanogen bromide, succinimide, aldehyde, tosyl chloride, avidin-biotin, epoxide, ~~and~~ maleimide, and carbodiimide~~, and~~

~~maintaining the contacting cells and composition under conditions and for a time sufficient to cause the cells to grow,~~

~~wherein the step of bringing into contact comprises administering the composition to a patient in need of cell growth~~.

15. The method of claim 14 wherein the composition is administered by injection, infusion, or implantation.

16. The method of claim 15 wherein the composition is administered by implantation of the composition and wherein the substrate is shaped to match a desired tissue shape.

17. The method of claim 16 wherein the substrate is biodegradable.

32. (Three times amended) ~~A~~ The method of claim 34 ~~testing a compound for an effect on tissue comprising~~

~~bringing into contact the compound to be tested and a composition comprising~~

~~a biocompatible solid substrate,~~

~~biocompatible polymeric tethers,~~

~~growth effector molecules, and~~

~~growing cells,~~

~~wherein one end of each tether is covalently linked to the substrate and each growth effector molecule is covalently linked to a distal end of a tether so that the growth effector molecule cannot be internalized by cells attached to the substrate, the growth effector molecules are attached to the substrate in a concentration effective to enhance the rate of target cell growth without internalization of the molecules, and the end of each tether covalently linked to the substrate is achieved using~~ an wherein the attachment agent is selected from the group consisting of cyanogen bromide, succinimide, aldehyde, tosyl chloride, avidin-biotin, epoxide,

~~and~~ maleimide, and carbodiimide~~; and wherein the growing cells are bound to the growth effector molecules;~~

~~incubating the compound and the composition under conditions promoting cell growth; and~~

~~observing the cells for any effect not observed in cells not brought into contact with the composition~~.

33. (new) A method for growing eukaryotic cells comprising

bringing into contact the cells with a composition comprising

a biocompatible solid substrate,

biocompatible polymeric tethers, and

growth effector molecules,

wherein one end of each tether is covalently linked to the substrate and one end is covalently linked to an growth effector molecule that the growth effector molecule cannot be internalized by cells attached to the substrate;

wherein the growth effector molecules are attached to the substrate in a concentration effective to enhance the rate of target cell growth without internalization of the molecules; and

wherein the tether is covalently linked to the substrate and to the growth effector molecule by the same attachment agents,

maintaining the cells in contact with the composition under conditions and for a time sufficient to cause the cells to grow.

34. (new) A method of testing a compound for an effect on tissue comprising

bringing into contact the compound to be tested and a composition comprising

a biocompatible solid substrate,

biocompatible polymeric tethers,

growth effector molecules, and

growing cells,

wherein one end of each tether is covalently linked to the substrate and one end is covalently linked to an growth effector molecule that the growth effector molecule cannot be internalized by cells attached to the substrate;

wherein the growth effector molecules are attached to the substrate in a concentration effective to enhance the rate of target cell growth without internalization of the molecules;

wherein the tether is covalently linked to the substrate and to the growth effector molecule by the same attachment agents; and

wherein the growing cells are bound to the growth effector molecules;

incubating the compound and the composition under conditions promoting cell growth; and

observing the cells for any effect not observed in cells not brought into contact with the composition.

Clean Version of Amended Claims

Pursuant to 37 C.F.R. § 1.121(c)(1)(ii)

14. (Three times amended) The method of claim 33

wherein the attachment agent is selected from the group consisting of cyanogen bromide, succinimide, aldehyde, tosyl chloride, avidin-biotin, epoxide, maleimide, and carbodiimide.

15. The method of claim 14 wherein the composition is administered by injection, infusion, or implantation.

16. The method of claim 15 wherein the composition is administered by implantation of the composition and wherein the substrate is shaped to match a desired tissue shape.

17. The method of claim 16 wherein the substrate is biodegradable.

32. (Three times amended) The method of claim 34 wherein the attachment agent is selected from the group consisting of cyanogen bromide, succinimide, aldehyde, tosyl chloride, avidin-biotin, epoxide, maleimide, and carbodiimide.

33. (new) A method for growing eukaryotic cells comprising

bringing into contact the cells with a composition comprising

a biocompatible solid substrate,

biocompatible polymeric tethers, and

growth effector molecules,

wherein one end of each tether is covalently linked to the substrate and one end is covalently linked to an growth effector molecule that the growth effector molecule cannot be internalized by cells attached to the substrate;

wherein the growth effector molecules are attached to the substrate in a concentration effective to enhance the rate of target cell growth without internalization of the molecules; and

wherein the tether is covalently linked to the substrate and to the growth effector molecule by the same attachment agents,

maintaining the cells in contact with the composition under conditions and for a time sufficient to cause the cells to grow.

34. (new) A method of testing a compound for an effect on tissue comprising

bringing into contact the compound to be tested and a composition comprising

a biocompatible solid substrate,

biocompatible polymeric tethers,

growth effector molecules, and

growing cells,

wherein one end of each tether is covalently linked to the substrate and one end is covalently linked to an growth effector molecule that the growth effector molecule cannot be internalized by cells attached to the substrate;

wherein the growth effector molecules are attached to the substrate in a concentration effective to enhance the rate of target cell growth without internalization of the molecules;

wherein the tether is covalently linked to the substrate and to the growth effector molecule by the same attachment agents; and

wherein the growing cells are bound to the growth effector molecules;

incubating the compound and the composition under conditions promoting cell growth; and

observing the cells for any effect not observed in cells not brought into contact with the composition.

ATL1 #574732 v1